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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/015,967	12/07/2001	Dan L. Eaton	P1447R1	9428

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EXAMINER	
JIANG, DONG	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 04/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/015,967	EATON ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33-43* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *33-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED OFFICE ACTION

Applicant's amendment filed on 05 December 2003 is acknowledged. Following the amendment, claims 33-40 are amended.

Currently, claims 33-43 are pending and under consideration.

Withdrawal of Objections and Rejections:

The objection of claims 33-40 under 37 CFR 1.821. (d) is withdrawn in view of applicant's amendment.

The prior art rejection of claims 33-38 and 40 under 35 U.S.C. 102(b) as being anticipated by Rosen et al. (WO 98/45712) is withdrawn in view of applicant's amendment.

Formal Matters:

Priority determination

This application claims priority to US provisional application 60/090,696, PCT/US99/12252, PCT/US00/08439, PCT/US00/23328, PCT/US01/06520, US applications 09/380,137, 09/709,238, and 09/941,992. The claimed priority has been denied for reasons of record set forth in the last Office Action, paper No. 13, mailed on 06 June 2003, i.e., none of the priority documents satisfies the utility/enablement requirement of 35 U.S.C. 101/112, first paragraph, and thus the present claims are not entitled to the benefit of the filling date of the prior applications.

Applicants argument filed on 05 December 2003 has been fully considered, but is not deemed persuasive for reasons below.

At pages 5-6 of the response, the applicant argues that the pending claims are entitled to at least the filing date of PCT/US00/23328 (8/24/00) as the '328 application discloses that the claimed polypeptide are differentially expressed in normal esophagus versus esophageal tumor tissue and rectum tumor tissue relative to normal rectum tissue (Example 18), showing that the polypeptides of the invention are useful diagnostically for the determination of the presence or absence of said tumors, and can be a useful target for the treatment of such tumors. This

argument is not persuasive for the reasons below. First, Example 18 is an experiment of quantitative PCR with cDNA libraries, which result does not represent the gene expression at the protein level as it is known in the art that the level of mRNA does not necessarily correlate to the level of protein expression. For instance, Haynes et al. (Electrophoresis, 1998, 19: 1862-1871) studied 80 proteins relatively homogenous in half-life and expression level, and found no strong correlation between protein and transcript levels, for some genes, equivalent mRNA levels translated into protein abundances which varied by more than 50 fold, and Haynes concluded that the protein levels cannot be accurately predicted from the level of the corresponding mRNA transcript (page 1863, the second paragraph of the left column, and Figure 1). Second, even if the mRNA level were used to predict the protein expression, PRO842 of the present invention are expressed in both normal and tumor tissues of esophagus and rectum, thus, it is unclear how significant the elevated level in rectum tumor tissue and reduced level in esophagus tumor tissue is, as there is no statistic analysis provided in the specification. Third, the experiment results were generated from *one* or more tissues of each, and it is unclear how many esophagus and rectum tissues were used for PRO842 detection, and it is impossible to conclude that a result generated from one sample is indicative for diagnostic uses. Finally, with respect to the asserted use in treating tumors, since it was unclear what was the actual biological function of PRO842, and whether PRO842 was the *causative* factor in esophagus and rectum tumors, and as the levels of PRO842 go up or down in different types of tumors based on very limited sample size, one of skilled in the art would not accept that PRO842 is a target for the treatment of such tumors, or would not know how to target PRO842 for therapeutic applications. Therefore, further research to identify or reasonably confirm a "real world" context of use is required for the claimed polypeptide. The changes in PRO842 levels in esophagus and rectum tumor tissues suggest a potential for diagnosis purpose, which, at the most, is an interesting invitation for further research and confirmation as it is not a practical method for "real world" use, and it requires significant further research and experimentation in order to form a useful and practical diagnosis method, which, by no means, is a routine or conventional experimentation. These further research and experimentation, however, is part of the act of invention, and until it has been undertaken, the asserted uses of PRO842 in diagnosis and treatment are not considered substantial utilities.

Claims

Applicant is advised that should claim 39 be found allowable, claim 40 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Objections and Rejections under 35 U.S.C. §112:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 33-37 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited in scope to a polypeptide of SEQ ID NO:2, and a polypeptide of SEQ ID NO:2 lacking its associated signal peptide, does not reasonably provide enablement for claims to various % variants SEQ ID NO:2, which do not have a functional activity, or do not have the same functional activity as SEQ ID NO:2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims, for the reasons set forth in the last Office Actions, paper No. 13, at pages 3-4.

Applicants argument filed on 05 December 2003, has been fully considered, but is not deemed persuasive for reasons below.

At page 7 of the response, Applicants argue that the present claims are fully enabled by the disclosure, that the Examiner has not established why a skilled artisan would have any difficulty selecting particular sequences falling within the scope of the claims that retain the biological activity of interest, and that a person of ordinary skill would require no more than routine experimentation to screen and select polypeptides that fall within the scope of the claims. This argument is not persuasive because the issue is not whether screening and selecting the functional polypeptides are routine or undue, rather, the issue is that the present claims

encompass inactive polypeptides as there is no functional limitation associated with the claimed polypeptide variants, and the specification does not teach how to use those inactive variants of SEQ ID NO:2. Therefore, undue experimentation would be required of the skilled artisan to determine the use of the inactive variants prior to use the claimed invention in its full scope.

Claims 33-37 remain further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons set forth in the last Office Actions, paper No. 13, at pages 4-5.

Applicants argument filed on 05 December 2003, has been fully considered, but is not deemed persuasive for reasons below.

At pages 8-9 of the response, Applicants argue that claims are directed to a finite range of polypeptide structures that are defined by reference to a particular polypeptide sequence, which has been fully described by the present specification, and that the applicant has described an intact, complete polypeptide having a particular biological significance and function, and presented claims to a range of structurally similar polypeptides using terms readily understood to a person skilled in the art. This argument is not persuasive because the present claims are drawn to a genus of polypeptides that is defined only by % sequence identity to a particular polypeptide sequence, and no particular conserved structure, or other disclosed distinguishing feature is required. Further, the specification does not disclose any structural and functional relationship of SEQ ID NO:2. As such, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides in reference to SEQ ID NO:2 based solely on % sequence identity, and the specification has not adequately described the claimed invention in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Rejections Over Prior Art:

The following rejections under 35 U.S.C. §§ 102 and 103 are made in view of the determination that the effective filing date for the instantly claimed invention is 07 December 2001, which is the actual filing date of the present application.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 33-42 remain rejected under 35 U.S.C. 102(b) as being anticipated by Lal et al., WO 200000610-A2 (06 Jan.-2000), for the reasons set forth in the last Office Actions, paper No. 13, at page 6.

Applicants argument filed on 05 December 2003, has been fully considered, but is not deemed persuasive for reasons below.

At page 10 of the response, Applicants argue that the current claims are entitled to a priority date of at least 8/24/00, and as such, the Lal reference is not prior art under 102(b). This argument is not persuasive for the reasons addressed above under "Priority determination".

Applicants further argue, at page 10 of the response, that the Lal reference is insufficient to be prior art to the presently claimed invention as it fails to enable one skill in the art to carry an invention into practical use. This argument is not persuasive because the statute of 102(b) itself merely requires that "the invention was patented *or described* in ...", and the present invention is directed to a product, an isolated polypeptide, which sequence was disclosed in the prior art reference. As such, the polypeptide of the present invention has been well described by the prior art reference, and the prior art reference meets the anticipating requirement of 102(b).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claim 43 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Lal et al., WO 200000610-A2 (06 Jan.-2000) as applied to claims 33-42 above, and further in view of Capon et al. (US 5,116,964), for the reasons set forth in the last Office Actions, paper No. 13, at pages 7-8.

Applicants argument filed on 05 December 2003, has been fully considered, but is not deemed persuasive for reasons below.

At page 14 of the response, Applicants argue that the current claims are entitled to a priority date of at least 8/24/00, and as such, the Lal reference is not prior art under 102(b). This argument is not persuasive for the reasons addressed above under "Priority determination".

Applicants further argue, at page 14 of the response, that the teachings of Capon fail to provide sufficient motivation or direction to modify the teachings of Lal to arrive at the subject matter of claim 43, and Capon does not suggest that polypeptides of the class or having a structure comparable to that of SEQ ID NO:2 could or should be modified in the manner that is claimed. This argument is not persuasive because Capon teaches indicates that fusion of a target protein (in general) to a stable plasma protein such as an immunoglobulin constant domain extends the in vivo plasma half-life, and facilitate purification of the protein, which clearly provides sufficient motivation to modify the polypeptide taught by Lal to make a fusion protein comprising Lal's polypeptide and an immunoglobulin Fc region following the teachings by Capon because, by doing so, it would extends the in vivo plasma half-life of the polypeptide, and facilitate purification of the protein.

With respect to that Capon does not suggest that polypeptides of the class or having a structure comparable to that of SEQ ID NO:2 could or should be modified in the manner that is claimed, it is the *combined* teachings of Lal and Capon, which allow the person of ordinary skill

in the art to make the chimeric polypeptide as claimed in claim 43. Otherwise, the Capon reference would have been an anticipating reference, and claim 43 would have been rejected under 35 U.S.C. 102 if the Capon reference had suggested polypeptides of the class or having a structure comparable to that of SEQ ID NO:2.

Conclusion:

No claim is allowed.

Advisory Information:

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on 571-272-0871. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Lorraine Spector

LORRAINE SPECTOR
PRIMARY EXAMINER

Dong Jiang, Ph.D.
Patent Examiner
AU1646
3/18/04